The results are illustrated at FIG. 1 and the following Table 1.

TABLE 1

Bioavailability of the test preparation of the present invention and the commercial product (SANDIMMUN^R)

Parameter	Control Prep. (A) M ± S.D. (n = 6)	Control Prep. (A) CV % (S.D./M)	Test Prep. (B) M ± S.D. (n = 6)	Test Prep. (B) CV % (S.D./M)	P-(B/A)
AUC (μg · hr/ml)	13.5 ± 9.9	73.3%	57.0 ± 16.5	28.9%	4.2
C_{max} (μg/ml)	0.8 ± 0.3	37.5%	6.2 ± 1.5	24.2%	7.8

Note:
AUC = Area under the blood concentration curve
C_{max} = Maximum blood concentration of cyclosporin
M ± S.D. = Mean value ± Standard deviation
CV = Ratio of standard deviation to mean value
P(B/A) = Ratio of mean value of the test preparation to mean value of the control preparation

As can be seen from the above table, the test preparation shows the increased AUC and C_{max} values which are about 4 times or more and about 7 times or more, respectively, as high as those of the control preparation. Accordingly, it can be identified that the bioavailability of the test preparation is significantly increased in comparison with that of the control preparation. In addition, the test preparation of the present invention exhibits an effect of decreasing the difference between respective test subjects (CV %) by about 2 times or more in AUC value and by about 1.5 times in C_{max} value, in comparison with the control preparation.

Accordingly, it could be determined that when the soft capsule composition according to the present invention is administered per oral, it shows the increased bioavailability of cyclosporin about 4 times as high as that of the prior commercial product containing ethanol, SANDIMMUN® Capsule and also a decrease of the difference between cyclosporin bioavailabilities in respective subjects, and at the same time, stably retains without any change during the long term storage. Thus, it is apparent that the microemulsion concentrate according to the present invention provides a significant improvement in the field of preparation of cyclosporin soft capsules.

EXAMPLE 9

To determine the particle-size distribution of the microemulsion which are formed by diluting the cyclosporin soft capsule composition of the present invention, which is prepared by using polyethylene glycol as a cosurfactant according to Example 1-2, and the commercial product SANDIMMUN® with water the microemulsions prepared therefrom were analyzed by means of a particle size analyzer (see Terence Allen Ph.D., Particle Size Measurement, Chapman and Hall, London, New York, 3rd Ed.). The results are shown in FIGS. **2** (SANDIMMUN®) and **3** (the composition of the present invention prepared according to Example 1-2).

As can be seen from FIGS. **2** and **3**, the average emulsified particle size of the preparation of Example 1-2 was about 0.1 μm and the average particle size of the commercial product SANDIMMUN® was 3.3 μm. Thus, it can be seen that the composition of the present invention can form the microemulsion having more micronized emulsified particle in comparison with the commercial product SANDIMMUN®. This result corresponds to that of Example 8 which demonstrates that the compositiion of the present invention provides a significantly increased bioavailability and a decrease of the difference between bioavailabilities in respective subjects. Accordingly, it is apparent that the composition of the present invention shows a significant improvement over the conventional commercial products in view of their emulsified state.

Although this invention has been described in its preferred form with a certain degree of particularity, it is appreciated by those skilled in the art that the present disclosure of the preferred form has been made only by way of example and that numerous changes in the details of the construction, combination and arrangement of parts may be resorted to without departing from the spirit and scope of the invention.

What is claimed is:

1. A cyclosporin-containing soft capsule composition which comprises:

(1) cyclosporin as an active ingredient,

(2) polyethylene glycol having a molecular weight of 200 to 600 as a cosurfactant,

(3) a mixture of an esterified compound of fatty acid and primary alcohol, medium chain fatty acid triglyceride and fatty acid monoglyceride as an oil component, and

(4) a surfactant having HLB (Hydrophilic-lipophilic balance) value of 10 to 17.

2. The cyclosporin-containing soft capsule composition of claim **1** wherein said cyclosporin is cyclosporin A.

3. The cyclosporin-containing soft capsule composition of claim **1** wherein said esterified compound of fatty acid and primary alcohol is an esterified compound of fatty acid having 8 to 10 carbon atoms and primary alcohol having 2 to 3 carbon atoms.

4. The cyclosporin-containing soft capsule composition of claim **3** wherein said esterified compound of fatty acid and primary alcohol is isopropyl myristate, isopropyl palmitate, ethyl linoleate or ethyl oleate.

5. The cyclosporin-containing soft capsule composition of claim **4** wherein said esterified compound of fatty acid and primary alcohol is ethyl linoleate.

6. The cyclosporin-containing soft capsule composition of claim **1** wherein said medium chain fatty acid triglyceride is caprylic/capric acid triglyceride.

7. The cyclosporin-containing soft capsule composition of claim **1** wherein said fatty acid monoglyceride is a monoglyceride of oleic acid.

8. The cyclosporin-containing soft capsule composition of claim **1** wherein the mixing ratio of fatty acid monoglyceride, the esterified compound of fatty acid and primary alcohol, and medium chain fatty acid triglyceride is 1:0–5:0.1–10 on the basis of weight.

9. The cyclosporin-containing soft capsule composition of claim **1** wherein said surfactant is a polyoxyethylene product of hydrogenated vegetable oil or a polyoxyethylene-sorbitan-fatty acid ester.

10. The cyclosporin-containing soft capsule composition of claim **9** wherein said surfactant is a mixed surfactant